REMARKS

Summary

The present invention is specifically directed towards a method of treating acute and chronic myeloid leukemia (AML & CML) and lymphoid leukemia, using a composition *consisting essentially of* a synergistic combination of chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ) in the ratio 1:1 to 1:10.

Status of the Claims

Sole independent claim 1 is proposed to be amended to emphasize the disclosed fact of a synergistic combination of CA and PCQ. Dependent claims 5, 11, 12, 14 and 15 have been amended to obviate informalities. Claim 18 is cancelled. Claims 1-17 now remain pending in the application, with Claim 1 being the sole independent claim. This application claims benefit to provisional application number 60/393,750, which results in an effective U.S. filing date of July 8, 2002.

Applicant points out hereafter that the final rejections of all claims should be reconsidered in view of 35 USC§ 103 (c) and should now be withdrawn. Applicant now offers a statement that removes the availability of Bandyopadhyay (PCT/1N00/00118) as prior art under 35 USC§ 102 (e), for purposes of supporting any type of obviousness rejection, as is permitted by 35 USC§ 103 (c).

Requested Action

Entry of this amendment, withdrawal of the final rejections and a Notice of Allowance are requested. Alternatively, entry to place the claims in better form for consideration on appeal is requested. No new issues are raised.

Substantive Rejection

All of the alternative rejections depend upon a single alleged teaching reference. Claims 1-4 and 6-18 have been finally rejected under 35 USC §103(a) as being unpatentable over an alleged primary teaching in Bandyopadhyay (PCT/1N00/00118) ['118 Document] in view of "applicants' admission". Claims 1-18 have been finally rejected under 35 USC §103(a) as being unpatentable over the '118 Document, in view of alleged secondary teachings in Zon et al (USP No. 5,700,927) ['927 patent] and further in view of alleged tertiary teachings in Bandyopadhyay et al. (USP Appln. Pub. No. 2003/0229140) ['140 Publication].

Response to the Substantive Rejection

The Examiner has relied upon an alleged primary teaching reference that is not a publication, but instead is the related, commonly-owned *application* Bandyopadhyay (PCT/1N00/00118), which has five named inventors, of which four are the same as those named in the present application. For clarity, Applicant attaches a copy of WO 02/45730 A1, published June 13, 2002, which is a published form of exactly what was disclosed in the application, Bandyopadhyay (PCT/1N00/00118). The first page of WO 02/45730 A1 confirms that it has the same assignee as the present application.

While not specified in the Final Rejection, the Examiner is understood to be relying upon the '118 Document as a prior art because it represents a "prior application by another" under 35 USC§ 102 (e) for purposes of constructing an obviousness rejection of all claims, under 35 USC§ 103 (a).

However, it is quite apparent from the documents of record that both the present

application and the '118 Document are patent application documents that are commonly assigned, and have overlapping inventive entities. Applicant hereby confirms that at the time the present invention was made, the subject matter of the '118 Document and the subject matter of the present invention were both owned by, or under an obligation of assignment to, Council of Scientific and Industrial Research. See, WO 02/45730 A1, attached.

Therefore, the '118 Document, as an earlier-filed, patent application by a slightly different inventive entity, involving subject matter also owned by Council of Scientific and Industrial Research at the time the present invention was made, categorically is not available as a "teaching" under 35 USC§ 102 (e) for purposes of then constructing an obviousness rejection of any of the claims to the present invention, using 35 USC§ 103 (a). This prohibition is pointed out specifically, in 35 USC§ 103 (c). See MPEP § 2146. Removal of the final rejections of all claims under 35 USC§ 103 (a) therefore respectfully is requested.

Whether or not the '118 Document, as an earlier-filed, patent application by a slightly different inventive entity, is able to be cited as a "prior art" teaching and then used as a basis for hypothesizing a 35 USC§ 103 (a) rejection, applicants hereafter once again emphasize that the broad disclosures of the '118 Document simply fail to present a *prima facie* case of obviousness. The '118 document teachings are certainly are less detailed than the "continuation-in-part" teachings found in U.S. Patent No. 6,852,344, which issued on an application filed on July 30, 2002, and emphasized only a polar extract of *Piper Betel* by HPLC, and specifically a composition including fractions nos. 1 and 9. The '344 Patent also has three inventors in common with the present application and that prior patent has been

obviated for purposes of "obviousness-type double patenting" by virtue of one of the Terminal Disclaimers of record.

The present inventors certainly are able to accurately characterize the teachings in the '118 Document, which has five named inventors, of which four are the same as those named in the present application. The Applicants previously made of record why the Examiner's assumptions are not supported by the actual teachings in the '118 Document, even if that prior application were to be assumed prior art as the "invention of another", under 35 USC §102(e), and available to be interpreted as a true "teaching reference" for purposes of an "obviousness" rejection, under 35 USC§ 103 (a).

Applicants offer the following additional comments against facts assumed in the final rejections, as stated, though such rejections will be moot, if the '118 Document is acknowledged to not be available under §102(e) for purposes of constructing an obviousness hypothetical, as pointed out by 35 USC§ 103 (c).

Contrary to the Examiner's stated, and completely hindsight starting point "Betel extract contains the compounds chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ)." such an oversimplification begs the question and hardly is a proper basis to reject Claims 1-4 and 6-18, either initially or finally, under 35 USC §103(a.)

Labeling a response as "unpersuasive" and repeating an initial rejection "as a courtesy" is not the same as considering a response and restating a *prima facie* case of obviousness in view of that response.

The '118 Document merely suggests use of a pharmaceutically effective amount of

betel leaf extract for treating myeloid leukemia in animal including human beings. The '118 Document reveals one particular type of Betel leaf extract but nowhere discloses the slightest awareness of which active compounds in betel leaf extract might form an essential part of a composition used in the treatment of acute and chronic myeloid leukemia (AML and CML).

Betel leaf extract contains a large number of compounds along with chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ). The inventors expended considerable amounts of time and effort in selectively identifying the two compounds namely chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ), from a pool of compounds present in Betel leaf extract, in a specific ratio showing an anti-leukemic and anti-tumor activity. Although inhibition of tumor promotion has been attributed to chlorogenic acid (CA), anti-tumor activity on established tumors including anti-leukemic activity has been particularly taught and distinctly claimed for the first time in the present invention.

Only the present specification identifies and presents positive data supporting the synergistic combination of the particular components, chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ), showing increased activity in treatment of AML, CML and lymphoid leukemia.

The '118 Document does not specifically teach any effective ratio of chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ) at which any effective composition should be administered to obtain the percentage growth inhibition of promonocyte cells, erythroleukemia cells or CML's leukemia cells as taught and claimed in the present invention .

Applicants strenuously disagree that the various dosage and growth inhibition results,

recited as limitations within claims 5 and 8-18, in particular, can be deemed "obvious" from anything recited within the four corners of the '118 Document. Characterizing a worker reading only the '118 Document as "imbued with at least a reasonable expectation that growth of cells ... would have been inhibited to some degree and the determination ... would be a matter well within the purview" is built upon the totally-unsupported assumption that the "compounds" particularly recited in all of claims 1-4 and 6-18 would be known by just reading the '118 Document. The Examiner appears to fully appreciate the '118 Document truly is inadequate, standing alone, to reject Claims 1-4 and 6-18, and therefore constructs an *alternative* final rejection, using alleged secondary and tertiary references.

Even assuming that the '118 Document could be characterized as §102 "prior art" it hardly is a proper "primary teaching reference" that in the alternative can be "modified" by alleged secondary and tertiary documents picked with hindsight, to support the *alternative* final rejection of all Claims 1-18, under 35 USC §103(a.) . First and foremost there is no recognition whatsoever as to anything other than "betel leaf" extract. The '118 Document does not even *mention* chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ), *let alone* "teach" or "suggest" what might be an "effective ratio" of CA and PCQ.

Labeling a response as "unpersuasive" and just repeating an alternative initial rejection "as a courtesy" is not the same as considering a response and restating a *prima facie* case of obviousness in view of that response.

First, no secondary teaching found in Zon et al (USP No. 5,700,927) ['927 patent] cures the essential deficiencies identified above in the '118 Document. The '927 patent merely

discloses and focuses upon substantially pure DNA encoding a Tbc1 polypeptide, a substantially pure Tbc1 polypeptide and methods of using such DNA to express Tbc1 in leukemic stem cells and treat certain leukemias. The '927 patent gives not even the slightest indication relating to whether a worker might recognize chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ) as compounds surprisingly effective together for treating acute and chronic myeloid leukemia (AML and CML) and lymphoid leukemia.

Second, and categorically, no tertiary prior art exists, as has been alleged by the Examiner! Bandyopadhyay et al. (USP Appln. Pub. No. 2003/0229140) ['140 Publication] is just not prior art.

The '140 Publication is by the same five inventors named herein; claims benefit to the same provisional application number 60/393,750 claimed herein which results in the same effective U.S. filing date of July 8, 2002; and was not published until December 11, 2003.

The '140 Publication, therefore, is simply irrelevant and cannot be relied upon to support the alternative, hypothetical rejection put forth by the Examiner.

The Examiner is thanked for indicating that the four Terminal Disclaimers filed with the January 3, 2007 Amendment are effective to eliminate any possibility of any continued "obviousness type double patenting" rejections.

Favorable reconsideration, withdrawal of the objections and rejections set forth in the Final Office Action, and an early Notice of Allowance are requested.

Any additional fee required to render this response timely may be charged to Deposit Acct. No. 06-1205. All correspondence should continue to be directed to the below-listed

address.

If questions remain prior to a Notice of Allowance, the Examiner is urged to telephone the undersigned attorney of record in our Washington, DC, at (202) 530-1010.

Respectfully submitted,

/warreneolsen/
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Attachment: Bandyopadhyay et al, WO 02/45730 A1 [App. No. PCT/1N00/00118]

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